REMARKS

Status of the Claims

Claims 24 and 28-49 are currently pending in the present application. Claims 1-23 and 25-27 have been canceled.

Claims 28 and 36 are withdrawn from consideration as being directed to a non-elected species. Thus, claims 24, 29-35, and 37-49 are currently being examined.

Rejections Under 35 U.S.C. § 102

A. Claims 24, 29-31, 35, 39-46, 48, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Konig *et al.* (WO 96/25435).

The claims as they stand are directed to a method of removing amyloid deposits from a patient comprising administering an immunoglobulin polypeptide or fragment thereof to the patient.

Konig *et al.* merely teach *in vitro* methods of labeling amyloid plaques present in the brain of a human patient, using immunohistochemical techniques involving monoclonal antibodies that bind beta-A4 peptide. The examiner asserts that Konig *et al.* generally discuss diagnostic and therapeutic uses of such antibodies in the diagnosis and treatment of Alzheimers diseases. Konig *et al.*, however, do not teach administration of antibodies to a patient for the removal of amyloid deposits as is claimed. In fact, Konig *et al.* do not even contemplate the use of the monoclonal antibody to remove amyloid fibrils from a patient as is claimed. Accordingly, on this issue alone, Konig *et al.* do not anticipate the claimed invention.

Applicants respectfully submit that the reference of Konig et al. also fails to provide a disclosure that enables the claimed methods. For instance, Konig et al. do not show that their monoclonal antibodies are effective for the removal of amyloid deposits as required by the claims. It is well settled that an anticipatory reference under 35 U.S.C. § 102 must also enable to claimed invention. For instance, the Federal Circuit has held that to anticipate, a reference must also enable one of skill in the art to make and use the claimed invention. See *Minnesota Manufacturing and Mining v. Chemque, Inc.*, 303 F.3d 1294 (Fed. Cir. 2002). Said another way, the reference must enable that which it is asserted to anticipate. *Elan Pharmaceuticals v. Mayo*

Foundation, 68 USPQ2d 1373, 1375 (Fed. Cir. 2003). Certainly, a general statement in Konig *et al.* that a monoclonal antibody "can be applied for the detection, monitoring, extraction, inhibition and modification of unique βA4 species, in the diagnosis and treatment of AD" cannot be held to be an enabling disclosure of a method of removing amyloid deposits in a patient as is currently claimed.

The Federal Circuit has set forth eight factors for enablement analysis of biological processes. The eight factors, often referred to as the "Wands factors" are (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). In considering the eight factors, Konig *et al.*, at a minimum, do not meet factors 2 and 3. Konig *et al.* do not provide specific direction or guidance to the currently claimed invention, a method for removing amyloid deposits in a patient. Further, Konig *et al.* do not provide working examples directed to *in vivo* removal of amyloid deposits.

Konig *et al.* provides nothing more than a general unsupported statement that the disclosed monoclonal antibodies could be used for the for treatment of AD. Further, as has already been demonstrated by applicants in the declaration of Dr. Biere submitted on October 23, 2002, the mere binding of an antibody to amyloid fibril for diagnostic purposes is not sufficiently predictive of its ability to remove amyloid fibril from a patient. Accordingly, the teachings of Konig *et al.* do not enable one of skill in the art to make and use the claimed invention and Konig *et al.* is not a reference under 35 U.S.C. § 102(b).

Applicants also note that claim 49 includes the limitation that the immunoglobulin polypeptide is a monoclonal antibody raised against an amyloid fibril. The antibody of Konig *et al.* is raised against beta-A4 peptide, not an amyloid fibril. Accordingly, Konig *et al.* do not disclose every element cited in the claim 49 and does not anticipate this claim, on this reason alone. Applicants respectfully request withdrawal of the rejection.

B. Claims 24, 29-35, and 37-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Becker *et al.* (EP 613007, David "Nettleship" Brems *et al.*).

As discussed above, the claims as they stand are directed to a method of removing amyloid deposits from a patient comprising administering an immunoglobulin polypeptide or fragment thereof to the patient.

Becker *et al.* generally discuss parenteral administration of antibodies having a specificity for beta-amyloid peptide in the beta-sheet conformation. Similar to Konig *et al.*, Becker *et al.* do not provide specific guidance or examples for administering such antibodies to remove amyloid deposits from patients. Accordingly, on this issue alone, Becker *et al.* do not anticipate the claimed invention.

Applicants also respectfully submit that Becker *et al.* also fail to provide a disclosure that enables the claimed methods. For instance, considering the Wands factors for enablement of biological processes, Becker *et al.*, at a minimum, do not meet factors 2 and 3. Like Konig *et al.*, Becker *et al.* do not provide specific direction or guidance to the currently claimed invention, a method for removing amyloid deposits in a patient. Further, Becker *et al.* do not provide working examples directed to *in vivo* removal of amyloid deposits.

As discussed in the declaration of Dr. Biere which was previously submitted, the mere binding of an antibody to amyloid fibrils for diagnostic purposes does not suggest that the antibody is able to remove amyloid fibrils from a patient. Becker *et al.* have not shown that their antibodies having specificity to beta-amyloid peptide are capable of removing amyloid fibrils from a patient. Respectfully, even if Becker *et al.* generally contemplate pharmaceutical compositions comprising their antibodies for parenteral administration, Becker *et al.* have not provided guidance for a method of administration of antibodies for removing amyloid fibrils from a patient. Since Becker *et al.* do not enable the anticipated invention , Becker *et al.* cannot anticipate the claims. Applicants respectfully request withdrawal of the rejection.

Applicants also note that claim 49 includes the limitation that the immunoglobulin polypeptide is a monoclonal antibody raised against an amyloid fibril. The antibody of Becker *et al.* is raised against beta- amyloid peptide, not an amyloid fibril. Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 103(a)

Claims 24, 29-35, and 37-49 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Konig *et al.* (WO 96/25435), Becker *et al.* (EP 613007, David "Nettleship" Brems *et al.*), and Benjamini *et al.* Ed. (Immunology: A Short Course).

As discussed above, the claims as they stand are directed to a method of removing amyloid deposits from a patient comprising administering an immunoglobulin polypeptide or fragment thereof to the patient.

The deficiencies of Konig *et al.* and Becker *et al.* are discussed above. Although Konig *et al.* and Becker *et al.* disclose antibodies that bind to beta-amyloid peptides, these references do not disclose a method of removing amyloid deposit from a patient comprising administering an immunoglobulin polypeptide or fragment thereof in an amount effective to remove amyloid deposits.

Benjamini *et al.* do not cure the deficiencies of Konig *et al.* and Becker *et al.* Benjamini *et al.* generally discuss opsonization of antigens by antibodies making them more attractive to phagocytic cells.

As discussed in Dr. Biere's declaration, the removal of amyloid deposits from a patient by administering antibodies to the patient is an unexpected discovery. At the time of the invention, antibodies have been successfully used as diagnostic tools in detecting the presence of amyloid deposits, but the use of antibodies to remove amyloid deposits from a patient was not known. None of these three cited references teach that antibodies could be used to remove amyloid deposits. Accordingly, the cited references do not render the claimed invention obvious and Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the accompanying remarks, Applicants respectfully request reconsideration and timely allowance of the pending claims. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact Applicants' undersigned representative to expedite prosecution.

If there is any fee due in connection with the filing of this Amendment, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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Dated: March 30, 2004

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